Inversion and computational maturation of drug response using human stem cell derived cardiomyocytes in microphysiological systems.

Journal: Sci Rep

Publication Year: 2018

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PubMed link: 30514966

Funding Grants: Human Cardiac Chip for Assessment of Proarrhythmic Risk

Public Summary:

Scientific Abstract:
While cardiomyocytes differentiated from human induced pluripotent stems cells (hiPSCs) hold great promise for drug screening, the electrophysiological properties of these cells can be variable and immature, producing results that are significantly different from their human adult counterparts. Here, we describe a computational framework to address this limitation, and show how in silico methods, applied to measurements on immature cardiomyocytes, can be used to both identify drug action and to predict its effect in mature cells. Our synthetic and experimental results indicate that optically obtained waveforms of voltage and calcium from microphysiological systems can be inverted into information on drug ion channel blockage, and then, through assuming functional invariance of proteins during maturation, this data can be used to predict drug induced changes in mature ventricular cells. Together, this pipeline of measurements and computational analysis could significantly improve the ability of hiPSC derived cardiomycocytes to predict dangerous drug side effects.